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Cognitive Reactivity, Dysfunctional Attitudes, and Depressive Relapse and Recurrence in Cognitive Therapy Responders

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Abstract

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Dr. Thase has served as a consultant to and was a member of various advisory boards for Eli Lilly and Company and received honoraria for talks sponsored by this company, which provided medication and matched placebo for use in a later phase of this research project. In addition to Eli Lilly and Company, during the past 2 years Dr. Thase has consulted with, served on advisory boards for, or received honoraria for talks from: Aldolor, Alkermes, AstraZeneca, Bristol-Myers Squibb Company, Dey, Forest Laboratories, GlaxoSmithKline, Janssen Pharmaceutica, Lundbeck, MedAvante, Inc., Merck, Neuronetics, Inc., Otsuka, PamLab, Pfizer Pharmaceuticals, PGx (now Forest), PharmaNeuroboost, Rexahn, Schering-Plough (now Merck), Shire US Inc., Supernus Pharmaceuticals, Transcept Pharmaceuticals, and Wyeth Pharmaceuticals (now Pfizer). During the past 2 years, he has received grant support from Eli Lilly and Company, Forest, GlaxoSmithKline, Otsuka, and Rexahn, in addition to funding from the National Institute of Mental Health and the Agency for Healthcare Research and Quality. He has equity holdings for MedAvante, Inc. and has received royalties from American Psychiatric Publishing, Inc. (APPI), Guilford Publications, Herald House, and W.W. Norton & Company, Inc. One book currently promoted by the APPI specifically pertains to cognitive therapy. Dr. Thase also discloses that his spouse is an employee of Embryon, Inc (formerly Advogent and Cardinal Health), which does business with several pharmaceutical companies that market medications used to treat depression.

Dr. Friedman has been a member of speaker bureaus or advisory boards for: AstraZeneca, Eli Lilly, GlaxoSmithKline, Pfizer, and Wyeth-Ayerst. Over the past five years, Dr. Friedman has received grant or research support from the following companies: Aspect Medical Systems, Indevus, AstraZeneca, Bristol-Myers Squibb, Pfizer, Sanofi-Aventis, Wyeth-Ayerst, Cyberonics, Novartis, NorthStar, and Medtronics.

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Dysfunctional attitudes can foreshadow depressive relapse/recurrence. Priming mood, through induction paradigms, is hypothesized to activate dysfunctional attitudes. Cognitive reactivity (CR) refers to mood-linked increases in dysfunctional attitudes after priming. Here we explored the extent to which CR as well as residual, *unprimed*, dysfunctional attitudes predicted depressive relapse/recurrence among depressed patients who responded to acute phase cognitive therapy (CT). Consenting adults, aged 18–70, with recurrent major depressive disorder (n = 523) participated in a two-site randomized controlled trial examining the durability of continuation phase treatments. Patients received 16–20 sessions of CT. Among the 245 incompletely remitted responders, 213 agreed to undergo a mood induction paradigm. After 8 months of continuation phase treatments, participants were followed an additional 24 months. Although the mood induction significantly lowered mood in 80% of responders, the expected CR was not evident. By contrast, higher *unprimed* dysfunctional attitudes following CT did predict relapse/recurrence over 20 and 32 months post randomization. The findings of this large longitudinal study of incompletely remitted CT responders challenge the notion that it is necessary to prime mood in order to maximize dysfunctional attitudes' prediction of relapse and/or recurrence. While findings cannot be generalized beyond CT responders, they emphasize the clinical importance of reducing dysfunctional attitudes in preventing depression.

Keywords

depression; cognitive therapy; cognitive reactivity; mood induction; dysfunctional attitudes

Major depressive disorder (MDD) remains one of the leading causes of disability worldwide (Üstün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004), affecting 13% of individuals (Hasin, Goodwin, Stinson, & Grant, 2005) to 16% (Kessler, Berglund, Demler, Jin, & Walters, 2005). Unfortunately, most people with depression will experience recurrent episodes of depression (Eaton, et al., 2008; Mattisson, Bogren, Horstmass, Munk-Jorgensen, & Nettelbladt, 2007). Risk for subsequent recurrence increases by 16 to 18% with each depressive episode (Mueller, et al., 1999; Solomon, et al., 2000). While no cure for MDD has been discovered, treatments including cognitive therapy (CT) can significantly reduce symptoms, and CT has been associated with a reduced risk for relapse (Vittengl, Clark, Dunn, & Jarrett, 2007).

An initial step toward targeting individuals at risk for relapse and recurrence for routine access to preventive treatments is to characterize and understand vulnerability. According to the most basic cognitive theories of depression, individuals vulnerable to depression preserve and overvalue negative and pessimistic assumptions about themselves, their futures, and the world (Clark & Beck, 1999). It is this cognitive triad of low self-esteem (self), hopelessness (future), and helplessness (world) (Moore & Garland, 2003) that typifies "cognitive vulnerability." Stressors can trigger these so called "silent assumptions," producing a cascade of automatic negative thoughts that characterize patients' thinking during depressive episodes (Beck, Rush, Shaw, & Emery, 1979).

Although the depressive assumptions can be easily assessed while individuals are depressed, negative cognitive processing can diminish during periods of remission (Ingram, Miranda, & Segal, 1998) and treatment. For example, Jarrett, Vittengl, Doyle and Clark (2007) showed that adults with recurrent MDD reported less negative cognitive content (measured by questionnaires) and 78.3% patients had scores in the "healthy" range *after being treated with CT.* Otto et al. (2007) found that dysfunctional attitudes distinguished never depressed and previously depressed women, even after controlling for residual depressive symptoms. These results, from a sample of 750 women who were not seeking treatment with CT, suggest that dysfunctional attitudes can be stable and may adequately mark vulnerability.

This pattern of findings underscore the need to understand the conditions under which different assessments of depressive cognitive content and processing can mark vulnerability and differentiate distinct patterns in the course of illness.

One such approach to assessment originated from the observation that dysphoric mood states stimulate negative cognitive processing (Clark & Beck, 1999; Persons & Miranda, 1992). This mood-state hypothesis relies on Bower's (1981) model of mood and memory, which suggests that mood, cognitions, and beliefs are mechanistically tied to recollections. A negative mood state elicits relevant memories, which then increases access to negative beliefs, cognitions, and attributions. A number of mood-induction procedures have been developed and tested (Van der Does, 2002; Westermann, Spies, Stahl, & Hesse, 1996). Verbal mood challenges in Miranda and Person's study (1988) of 43 women with a low current level of depressive symptoms (i.e., Beck Depression Inventory [BDI; (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961)] scores ≤ 13), worsened both mood and cognitive content as measured by the Multiple Affect Adjective Checklist (MAACL; (Zuckerman & Lubin, 1965) and the Dysfunctional Attitudes Scale (DAS; (Weissman, 1979), respectively. Further, women with a history of MDD had higher DAS scores than those without. Similar findings were observed in a larger study of 100 not currently depressed women using a different mood induction procedure (i.e., watching a sad film clip; Miranda et al., 1998). These findings support the hypothesis that provocations that lower mood can also "activate" or increase levels of the dysfunctional attitudes.

Other lines of research have shown that additional cognitive processes, including rumination (Huffziger & Kuehner, 2009; Kuehner, Liebsch, & Huffziger, 2009; Singer & Dobson, 2007), affective reactivity (Cohen, Gunthert, Butler, O'Neill, & Tolpin, 2005), and attentional bias (Beevers & Carver, 2003; Green, Sedikides, Saltzberg, Wood, & Forzano, 2003), are also mood-state dependent. The mood-state dependent change in dysfunctional attitudes, or cognitive reactivity (CR), has been linked to dysphoria (Wenze, Gunthert, & Forand, 2007) and again has discriminated previously depressed from never depressed individuals (Mongrain & Trambakoulos, 2007). In a prospective test of the predictive validity of CR, Segal et al. (2006) followed 99 recently remitted outpatients over an 18-month period and found that CR was associated with an increased risk of relapse or recurrence. Further, patients who had been treated with antidepressant medication had greater CR than did those who had been treated with CT.

Here we explore the role of cognitive reactivity in predicting relapse and recurrence in a large sample of patients with a recurrent MDD who responded to CT and who were followed for up to 32 months. The unique aspect of this analysis is that we will evaluate CR in a large sample of CT responders who continue to be at higher risk for relapse and recurrence and follow this at-risk patient group for 32 months after acute phase CT. We predicted that patients who exhibited greater CR after CT would be more likely to relapse and/or recur, both over an 8-month continuation treatment phase and a 24-month protocol treatment-free follow-up.

Method

Participants

Patients (n = 523) consented to participate in a two site (The University of Pittsburgh and The University of Texas Southwestern Medical Center) Institutional Review Board-approved randomized controlled trial of continuation phase therapies following acute phase CT (Jarrett & Thase, 2010). Included adult outpatients were between the ages of 18 and 70, spoke English, could complete study visits and assessments, and met the following criteria: (a) were diagnosed with DSM-IV non-psychotic, recurrent MDD by evaluators utilizing the

Structured Clinical Interview for Depression (SCID-I; First, Spitzer, Gibbon, & Williams, 1996); (b) were remitted between depressive episodes, had at least one prior episode with complete inter-episode recovery, or had antecedent dysthymic disorder; and (c) had a score of ≥ 14 on the 17-item Hamilton Rating Scale for Depression ($HRSD_{17}$; Hamilton, 1960; Williams, 1988). Exclusion criteria included: (a) medical disorders or treatments that can cause depressive symptoms; (b) concurrent DSM-IV psychiatric disorders such as bipolar disorder, active alcohol or substance dependence, primary (predominant) obsessive compulsive disorder or eating disorders, or psychotic or organic mental disorders; (c) active suicidal risk; (d) prior treatment failure of an adequate trial of CT or fluoxetine; (e) inability to complete questionnaires in English; (f) pregnancy or planning a pregnancy during the first 11 months on study; or (g) failure to provide informed consent.

Patients included in the current analysis (a) had "responded" to either 16 or 20 sessions of acute phase CT for MDD over the course of 12 – 14 weeks; (Response was defined by an independent evaluator as no MDD and $HRSD_{17}$ ≤12) and (b) were delineated as being higher risk by the presence of at least one $HRSD_{17}$ score ≥ 7 during the last seven acute phase evaluations, including the blind evaluation. Of the 241 higher risk patients randomized to continuation phase treatments, 213 consented to the mood induction procedure (MIP; defined below). Due to missing data, analyses were based on 207 patients.

We also analyzed data from 43 lower risk (absence of any $HRSD_{17}$ score ≥ 7 during the last seven acute phase evaluations) patients. The results are not reported as they are similar to those for the higher risk patients.

The analyzed sample had an average age of 42.9 (SD = 11.9) years, with a mean of 15.5 (SD = 2.9) years of education; 66.2% were women, and 57.5% were single; and 86.5% were White, 7.8% were Black, 2.9% Hispanic, and 2.4% were Other. See Table 1 for additional patient demographic and clinical characteristics.

Procedures

Following acute phase CT, responders meeting the definition for higher risk were randomized to one of three continuation phase therapy conditions within the 8-month experimental phase: continuation phase CT (C-CT), fluoxetine (FLX; up to 40 mg/day), or an identically appearing inert pill placebo (PBO). Blinded evaluations occurred every 4 months during the experimental phase as well as during the subsequent 24 months of follow-up. Evaluators blinded to cell assignment assessed patients for relapse or recurrence (defined under Primary Outcome) at each evaluation. The MIP was administered at the first, third and ninth blinded evaluations, which occurred at randomization, the end of the experimental phase, and the completion of follow-up, respectively. The MIP administered at the first blinded evaluation was used in the test of the primary hypothesis below.

Mood Induction Procedure

Patients sat in a quiet room and first completed the Visual Analogue Scale (VAS) and then either the DAS-A or DAS-B; the presentation pre MIP or post MIP order of DAS Forms A and B was randomly counterbalanced across patients and blinded evaluations. The evaluator then read:

> "You are about to listen to a not particularly happy piece of music. It is meant to create a temporary sad mood. We would also like you to recall a sad event or memory from your life and then think about it while you listen to the music. Music can be a very personal thing and it may affect people differently. To help create a sad mood, however, please try to think about, or notice, the sadness in the music as

you continue to think about the sad event or memory. The tape takes about 10 minutes to complete."

The music used for the MIP was "Russia Under the Mongolian Yoke" by Prokofiev, which was re-mastered to play at half speed for about 8 minutes. This orchestral piece was first used by Clark and Teasdale (1985) and has been found to be an effective mood challenge by others (Lethbridge & Allen, 2008; Segal, Gemar, & Williams, 1999). During the early years of the study, the recording was played via audio cassette tape and later through computer speakers from a digital recording; volume was adjusted according to patient preference.

When the music stopped, the patient completed another VAS, the alternate DAS form, and a final VAS. The evaluator then debriefed the patient, documented that the patient's negative mood had dissipated, and address questions or concerns.

At the end of the MIP, the evaluator met with the patient for debriefing and conducted a semi-structured interview regarding the effect of the MIP on the patient's mood. The interviewer included the following Yes/No questions and gave patient an opportunity to elaborate: "Did the manipulation have an effect? Did you allow yourself to feel as sad as the task could potentially have made you feel? Did you distract yourself by thinking of non-related things? Did you use coping skills that you learned in therapy?"

Assessment

Measures

Visual Analog Scale (VAS; Gemar, Segal, Sagrati, & Kennedy, 2001): Patients self-reported mood by marking an "x" on a continuous line with fixed-end anchor descriptors of "happy" on the right and "sad" on the left. All distances were measured from the left end of the line, with lower measurements indicating more intense sadness, and higher measurements indicating more intense happiness. Although the original VAS was 156 mm, this study used a 100 mm scale, which has been reported to be as accurate as the original (Bowen, Clark, & Baetz, 2004; Lethbridge & Allen, 2008; Marzillier & Davey, 2005; Scherrer & Dobson, 2009).

Dysfunctional Attitudes Scale (DAS; Weissman, 1979): The DAS assesses an individual's "silent assumptions" about himself or herself. The self-report 40-item measure asks patients to rate statements on a 7-point Likert Scale, with higher scores indicating both a greater number and larger severity of dysfunctional beliefs. The scale demonstrated high internal consistency (e.g. .93 to .96; Beevers, Strong, Meyer, Pilkonis, & Miller, 2007). The current report makes use of two assessments of DAS at the first blinded evaluation; mean alpha internal consistency was .94 (median = .94, range .93 – .94).

Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960): The $HRSD_{17}$assesses symptom severity of individuals already diagnosed with MDD. The 17 items are rated on 3- or 5-point scales by clinicians; higher scores indicate greater symptom severity. Strong inter-rater reliability (r = .85) and convergent validity (rs = .70 – .83) have been established (Clark & Watson, 1991). Ratings for depression severity were calibrated among evaluators inter- and intra-site regularly for the duration of the study, as detailed in Jarrett & Thase (2010). The current report makes use of two assessments from the diagnostic phase through randomization; mean alpha internal consistency was .69 (median = .71, range .45 – .85).

Longitudinal Interval Follow-up Evaluation- Psychiatric Status Ratings (LIFE-PSR; Keller, Shapiro, Lavori, & Wolfe, 1982B): The LIFE-PSR, one of three sections of the semi-structured LIFE interview, longitudinally tracks DSM-IV Axis I disorders, which are assessed retrospectively in weekly intervals. The psychometric properties of the LIFE-PSR

have been established with the following findings. The LIFE-PSR has excellent reliability with interclass correlation coefficients of at least Cronbach's α = .90 (Keller, et al., 1987). Adequate external validity (r = −.45 to −.57) has been found using scales such as the Global Assessment of Functioning (GAF; American Psychiatric Association, 1994) and the Medical Outcomes Study (MOS; Stewart, Hays, & Ware, 1988). For this analysis, only the PSRs for DSM-IV MDD were used. Major Depressive Disorder was assessed on a 6-point scale, with higher scores indicating greater symptom severity; episode duration was also recorded. In the current dataset, the median of the lag 1 autocorrelations is 0.87, which shows good week-to-week consistency in evaluators' ratings within each patient.

Evaluators—Independent clinical evaluators unaware of treatment assignment or higher and lower risk strata conducted the interviews and scored the LIFE-PSR. Research personnel who did not treat the patients administered the MIP.

Primary Outcome—Relapse, recurrence, and recovery were defined by the LIFE-PSR assessments. Relapses and recurrences were operationalized as LIFE-PSR scores ≥ 5 for 2 consecutive weeks. Depressive episodes were considered relapses if they occurred prior to meeting criteria for recovery, and recurrences if they occurred following recovery. Recovery was defined by 35 consecutive weeks of remission (i.e., LIFE-PSR scores ≤ 2).

Statistical Analyses

We used repeated measures analysis of variance methods to compare mean levels of mood and DAS scores between pre- and post-mood induction procedures. Pearson's product moment correlation coefficient estimated the linear association between mood change and change in dysfunctional attitudes between pre- and post-mood induction procedure. Cox proportional hazard regression analysis assessed the extent to which higher DAS scores predicted relapses and recurrences over the experimental and follow-up phases. Descriptive statistics summarize the findings from the debriefing session.

Results

To ensure that the MIP had the expected impact on mood, we examined both the mean change in mood and the change among patients who experienced a mood worsening. The MIP significantly decreased mood at the end of acute phase therapy, with the mean (SD) VAS score decreasing from 68.3 (16.9) to 51.0 (20.2) (repeated measures ANOVA $F_{1, 206}$ = 167.4, $p < .001$) (see Table 2). Of note, about 20% ($n = 41$) of patients experienced either a paradoxical improvement in mood ($n = 34$) or no change in mood ($n = 7$). Among those whose mood worsened, the mean (SD) VAS score after the mood induction procedure was 47.6 (19.1), which was significantly lower than the pre-mood induction mean of 70.0 (16.0) (repeated measures ANOVA $F_{1,165} = 250.5$, $p < .001$). Please refer to Table 2 for details.

The hypothesis that the MIP would elicit an increase in dysfunctional attitudes was, by contrast, unsubstantiated. There was no significant change in pre- and post-mood induction mean levels of DAS scores. Interestingly, the MIP produced a significant reduction in dysfunctional attitudes for the 20% of patients with improved or unchanged mood at the first blinded evaluation. Table 3 details these changes.

Although not part of our original data analytic plan, we also examined the relationship of change in DAS scores (dependent variable) and VAS mood ratings (covariate), using a. repeated measures ANCOVA . Consistent with the findings of the primary analyses, the mood induction procedure did not produce a significant change in DAS scores (ANCOVA Time Effect: F1, 205 = 3.78, p = .053), at the a priori alpha level we set. There was, however, a significant time × change interaction in VAS score effect (F1, 205 = 10.57, p = .

001) suggesting that patients who experienced higher levels of mood change also experienced a greater change in DAS scores.

The results from the post MIP debriefing follow. Only 19% (8 of 41) of patients whose mood was unchanged or improved commented that the MIP had no effect. On the other hand, a significantly higher proportion of patients (65% or 102 of 158, chi-square = 26.7, p-value < .001) whose mood worsened after MIP claimed to have been affected by the MIP. Only 39% (45 of 114) patients with worsened mood commented that they allowed the MIP to make them feel sad. This was not significantly different from 50% (9 of 18) of patients with an unchanged or improved mood who had a similar comment about allowing MIP to make them feel sad (Fisher's exact test p-value = .45). Thirty eight percent (13 of 34) of patients whose mood was unchanged or improved commented that they distracted themselves by thinking of "non-related things" compared to 44% (51 of 116) with worsened mood after MIP. Overall, 52% (91 of 174[1]) of the total sample stated that that during the MIP they used coping skills learned in therapy. Specifically, 54.8% (74 of 135) patients with worsened mood and 43.6% (17 of 39) patients with unchanged or improved mood reported to have used coping skills learned in therapy.

Because we did not observe the hypothesized negative cognitive reactivity, we examined the extent to which an *unprimed* DAS scores at the end of acute phase therapy predicted relapse and/or recurrence. These DAS scores did not predict relapse during the 8-month continuation phase (i.e., FLX, PBO, or C-CT). However, these *unprimed* DAS scores following acute phase CT were predictive of relapse and/or recurrence across both the first year (20 months post-randomization) and second year of follow-up (i.e., full 32 months post randomization). We reported 20 months year post randomization as well as 32 months post-randomization (i.e., post CT) to be consistent with relapse/recurrence estimates in the literature and in the overall design of this trial). In particular, after controlling for post-treatment depression severity (as measured by $HRSD_{17}$ at randomization, patients with higher DAS score were at greater risk of relapse/recurrence over 20 months [$\chi^2 = 3.93$, $p < .047$, hazard ratio (HR) = 1.01] and over 32 months post-randomization [$\chi^2 = 4.49$, $p < .034$, hazard ratio (HR) = 1.01] after completion of acute phase CT as compared to patients with a unit lower DAS score. Thus, patients with one SD (SD = 30.2) higher DAS score had a 1.33 times higher risk of relapse/recurrence [HR = 1.33, 95% CI: 1.32, 1.35] over 20 months post-randomization. A similar increase in risk was also observed over 32 months post-randomization [HR = 1.32, 95% CI: 1.30, 1.33]. Details are given in Table 4. Neither statistical significance nor the direction of the effect changed after replacing pre-MIP DAS scores with post-MIP DAS scores. Note, neither the type of continuation phase treatment (i.e., PBO, FLX, CCT) nor the interaction of treatment with pre-MIP DAS scores were statistically significant; thus these effects not reported.

Finally, we found that the direction of mood change after MIP did not influence the rates of relapse or recurrence. We have estimated the relapse/recurrence rates using Kaplan-Meier method for patients with worsened and unchanged or improved mood after MIP and compared them using a log-rank test. The results suggest that the direction of mood change was not protective (or provocative) in terms relapse and/or recurrence. Details are in Table 5.

Discussion

We found that 80% of patients with recurrent major depression, who had responded to acute phase CT and were at higher risk for relapse marked by unstable remission, reported

[1]Sample sizes vary due to missing data (i.e., patient non-response during debriefing).

lowered mood after a standard MIP. Contrary to the prediction, however, the MIP did not increase dysfunctional attitudes compared to pre-provocation. Indeed, the only evidence of cognitive reactivity observed was among a subset of patients who experienced a paradoxical mood *elevation* following MIP, who also experienced a reduction in DAS scores. Importantly, because no clear evidence of negative cognitive reactivity was detected, it was impossible to test the hypothesis that CR would be associated with risk of relapse/recurrence. We do acknowledge that a post hoc analysis showed a trend for patients who experienced higher levels of mood change to also evidence a greater change in DAS scores.

At the same time, the unprimed DAS scores at the end of acute phase therapy did predict relapse/recurrence rates over the subsequent 32 months, consistent with previous findings (Alloy, Abramson, Walshaw, & Neeren, 2006; Rush, Weissenburger, & Eaves, 1986).

The apparent discrepancy in results of this study and those of Segal et al. (2006), Miranda and Persons (1988) and others may be due to this sample consisting *only of CT responders* who presented with recurrent MDD. One limitation is of our study did not include people with only a single lifetime episode of depression, nor did we recruit a healthy control group. Miranda and Persons (1988) and others (Gemar, et al., 2001; Miranda, et al., 1998) found that CR distinguished people with a history of depression from never-depressed individuals; no such comparison was part of the higher risk stratum. The fact that CR was not evident in the current study suggests that the CT responders may have been activating a behavior or a yet to be identified skill, perhaps learned in cognitive therapy, that prevented an increase in dysfunctional thoughts even in the presence of a negative affect shift. Consistent with this speculation were the findings that the assignment to continuation phase treatment did not influence the results of the MIP, suggesting that the operative mechanism may be occurring in the acute phase of CT at least among responders. Also consistent with this speculation are the findings of Segal et al. (1999; 2006[2]), who observed that patients who had recovered from MDD with CT treatment exhibited less CR than those who recovered with pharmacotherapy. Together, this set of studies underscores the potential importance of treatment modality and possibly their distinct, inherent mechanisms of change, particularly in relation to CR.

Clark and Beck (1999) suggested that elevated DAS scores may simply be a proxy for residual depressive symptoms in partially remitted patients rather than an independent forecaster of relapse and recurrence. Because higher risk patients were identified by not experiencing a sustained remission by the end of acute phase CT, we also examined the predictive value of DAS scores after controlling for depression severity as measured by the $HRSD_{17}$ at randomization. After taking level of depressive symptoms into account, the DAS at both pre- and post-MIP continued to predict relapse/recurrence risk: for each unit increase in DAS score, the likelihood of relapse and or recurrence increases by one percent. Given the large range (i.e., 40 – 280) of possible DAS scores, a unit increase in DAS score change may appear to be clinically insignificant. Nevertheless, a 20 or 30 point difference in DAS scores would be associated with a large, clinically relevant difference in depressive vulnerability. Indeed, in the current sample, one SD (30 points) increase in the DAS was associated with 1.33-fold increase in the risk of relapse/recurrence over 20 months post-randomization which appears clinically significant.

An unexpected and interesting finding was that 20 percent of our patients demonstrated a more positive mood following the negative mood induction procedure. These patients also experienced a significant decrease in dysfunctional attitudes, or “positive cognitive

[2]A logistic regression of Segal et al. 2006 data showed that controlling for HRSD score at pre-MIP, the unprimed or (pre MIP) DAS scores did not predict relapse and recurrence at 18 months post randomization.

reactivity," following the first MIP (at the end of acute phase). Thirty-eight percent of patients with unchanged or improved mood after MIP did not follow the directions and reported that they distracted themselves by thinking of things unrelated to the instructions. Some patients also reported that they were able to focus on the more relaxing aspects of the music. In addition, 43.6% of these patients reported using skills learned during therapy. Wenze, Gunthert, and Forand (2007) suggested that positive cognitive reactivity, or positive affectivity in association with positive mood, may serve as a protective factor against developing depressive symptoms. While the debriefing results above do not describe all the patients with positive mood shifts, some patients were able to affectively or cognitively neutralize music that lowered mood in most other CT responders. The extent to which this positive CR phenomenon can be replicated or associated with relapse and recurrence requires study in samples evidencing a higher percentage of positive CR.

Our study has a number of important limitations. As mentioned previously, all patients responded to CT and were not compared to other treatment groups or to patients in distinct states of remission or recovery. The reported results cannot be generalized beyond CT responders who presented with recurrent MDD, and were higher risk for relapse and recurrence due to unstable remission in the late stage of acute phase CT. Other limitations follow. Approximately 11.6% (28 of 241) of higher risk randomized responders did not grant consent to the mood induction procedure, and 2.5% (6 of 213) of higher risk randomized who consented to MIP were omitted due to missing data. Further, if the MIP was conducted prior to and during acute phase CT in the current sample, we could more fully examine CT's effect on CR.

Because we hypothesize that some type of compensatory strategy, or cognitive therapy skill, may have prevented CR, the effect of skill mastery on the level of change in dysfunctional attitudes should be further explored. Barber and DeRubeis (2001) discovered, albeit in a small sample, a significant inverse correlation between DAS scores and the Ways of Responding Scale (WOR), indicating that as CT skills increase, dysfunctional attitudes decrease. We will have a chance to investigate the potential moderating effects of the DAS with a measure designed to capture both skill acquisition and usage during CT (i.e., the Skills of Cognitive Therapy scale; (SoCT; Jarrett, Vittengl, Thase, & Clark, 2011).

In summary, our findings suggest that the absence of CR following treatment may be specific to CT responders. This interpretation is in line with Segal et al. (2006), who demonstrated that CT responders exhibited diminished CR compared to patients who received pharmacotherapy or pill placebo. Findings challenge the idea that it is necessary to prime mood in order to maximize dysfunctional attitudes' prediction of depressive relapse and/or recurrence. While the findings may be specific to incompletely remitted CT responders, they emphasize the clinical importance of restructuring dysfunctional attitudes in preventing relapse and recurrence. Future research may examine the change in cognitive reactivity (both positive and negative) throughout the course of illness before, during, and following different modalities of treatment.

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References

Alloy LB, Abramson LY, Walshaw PD, Neeren AM. Cognitive vulnerability to unipolar and bipolar mood disorders. Journal of Social and Clinical Psychology. 2006; 25(7):726–754.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4. Washington, DC: American Psychiatric Association; 1994.

Barber JP, DeRubeis RJ. Change in compensatory skills in cognitive therapy for depression. Journal of Psychotherapy Practice & Research. 2001; 10(1):8–13. [PubMed: 11121002]

Beck, AT.; Rush, AJ.; Shaw, BF.; Emery, G. Cognitive therapy of depression. New York: Guilford Press; 1979.

Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Archives of General Psychiatry. 1961; 4:561–571. [PubMed: 13688369]

Beevers CG, Carver CS. Attentional bias and mood persistence as prospective predictors of dysphoria. Cognitive Therapy and Research. 2003; 27(6):619–637.

Beevers CG, Strong DR, Meyer B, Pilkonis PA, Miller IW. Efficiently assessing negative cognition in depression: An item response theory analysis of the Dysfunctional Attitudes Scale. Psychological Assessment. 2007; 19(2):199–209. [PubMed: 17563201]

Bowen R, Clark M, Baetz M. Mood swings in patients with anxiety disorders compared with normal controls. Journal of Affective Disorders. 2004; 78:185–192. [PubMed: 15013242]

Bower GH. Mood and Memory. The American Psychologist. 1981; 36(2):129–148. [PubMed: 7224324]

Clark, DA.; Beck, AT. Scientific Foundations of Cognitive Theory and Therapy of Depression. New York: John Wiley; 1999.

Clark DM, Teasdale JD. Constraints of the effects of mood on memory. Journal of Personality and Social Psychology. 1985; 28:1595–1608.

Clark LA, Watson D. Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. Journal of Abnormal Psychology. 1991; 100:316–336. [PubMed: 1918611]

Cohen LH, Gunthert KC, Butler AC, O'Neill SC, Tolpin LH. Daily affective reactivity as a prospective predictor of depressive symptoms. Journal of Personality. 2005; 73(6):1–27. [PubMed: 15660671]

Eaton WW, Shao H, Nestadt G, Lee BH, Bienvenu J, Zandi P. Population-based study of first onset and chronicity in Major Depressive Disorder. Archives of General Psychiatry. 2008; 65(5):513–520. [PubMed: 18458203]

First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JB. Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P, Version 2.0). New York: New York State Psychiatric Institute, Biometrics Research Department; 1996.

Gemar MC, Segal ZV, Sagrati S, Kennedy SJ. Mood-induced changes on the Implicit Association Test in recovered depressed patients. Journal of Abnormal Psychology. 2001; 10(2):282–289. [PubMed: 11358022]

Green JD, Sedikides C, Saltzberg JA, Wood JV, Forzano LB. Happy mood decreases self-focused attention. British Journal of Social Psychology. 2003; 42:147–157. [PubMed: 12713761]

Hamilton M. A rating scale for depression. Journal of Neurology, Neurosurgery & Psychiatry. 1960; 23:56–62.

Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of Major Depressive Disorder: Results from the National Epidemiologic Survey on Alcoholism and Related Conditions. Archives of General Psychiatry. 2005; 62(10):1097–1106. [PubMed: 16203955]

Huffziger S, Kuehner C. Rumination, distraction, and mindful self-focus in depressed patients. Behaviour Research and Therapy. 2009; 47(3):224–230. [PubMed: 19166993]

Ingram, RE.; Miranda, J.; Segal, ZV. Cognitive Vulnerability to Depression. New York: Guilford Press; 1998.

Jarrett RB, Thase ME. Comparative efficacy and durability of continuation phase cognitive therapy for preventing recurrent depression: Design of a double-blinded, Fluoxetine- and pill-placebo–controlled, randomized trial with 2-Year follow-up. Contemporary Clinical Trials. 201010.1016/j.cct.2010.04.004

Jarrett RB, Vittengl JR, Doyle K, Clark LA. Changes in cognitive content during and following cognitive therapy for recurrent depression: Substantial and enduring, but not predictive of change in depressive symptoms. Journal of Consulting and Clinical Psychology. 2007; 75(3):432–446. [PubMed: 17563160]

Jarrett RB, Vittengl JR, Thase ME, Clark LA. Skills of Cognitive Therapy (SoCT): A new measure of patients' comprehension and use. Psychological Assessment. 2011

Keller MB, Lavori PW, Friedman B, Nielson E, Endicott J, McDonald-Scott P, et al. The Longitudinal Interval Follow-up Evaluation: A comprehensive method for assessing outcome in prospective longitudinal studies. Archives of General Psychiatry. 1987; 44(6):540–548. [PubMed: 3579500]

Keller MB, Shapiro RW, Lavori PW, Wolfe N. Relapse in major depressive disorder: Analysis with the life table. Archives of General Psychiatry. 1982b; 39(8):911–915. [PubMed: 7103680]

Kessler RC, Berglund P, Demler O, Jin R, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry. 2005; 62(6):593–602. [PubMed: 15939837]

Kuehner C, Liebsch K, Huffziger S. Research letter: Emotional Reactivity to induced rumination predicts 1-year level of depressive symptoms. Psychological Medicine. 2009; 39:1226–1228. [PubMed: 19368746]

Lethbridge R, Allen M. Mood-induced cognitive and emotional reactivity, life stress, and the prediction of depressive relapse. Behavior Research and Therapy. 2008; 46:1142–1150.

Marzillier SL, Davey GCL. Anxiety and disgust: Evidence for a unidirectional relationship. Emotion. 2005; 19(5):729–750.

Mattisson C, Bogren M, Horstmass V, Munk-Jorgensen P, Nettelbladt P. The long-term course of depressive disorders in the Lundby Study. Psychological Medicine. 2007; 37:883–891. [PubMed: 17306047]

Miranda J, Gross JJ, Persons JB, Hahn J. Mood matters: Negative mood induction activates dysfunctional attitudes in women vulnerable to depression. Cognitive Therapy and Research. 1998; 22(4):363–376.

Miranda J, Persons JB. Dysfunctional attitudes are mood-state dependent. Journal of Abnormal Psychology. 1988; 97:76–79. [PubMed: 3351115]

Mongrain M, Trambakoulos J. A musical mood induction alleviates dysfunctional attitudes in needy and self-critical individuals. Journal of Cognitive Psychotherapy. 2007; 21(4):295–309.

Moore, RG.; Garland, A. Cognitive Theory for Chronic and Persistent Depression. West Sussex: John Wiley & Sons; 2003.

Mueller TI, Leon AC, Keller MB, Solomon DA, Endicott J, Coryell W, et al. Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. American Journal of Psychiatry. 1999; 156(7):1000–1006. [PubMed: 10401442]

Otto MW, Teachman BA, Cohen LS, Cohen CN, Vitonis AF, Harlow BL. Dysfunctional attitudes and episodes of major depression: Predictive validity and temporal stability in never-depressed, depressed, and recovered women. Journal of Abnormal Psychology. 2007; 116(3):475–483. [PubMed: 17696703]

Rush AJ, Weissenburger J, Eaves G. Do thinking patterns predict depressive symptoms? Cognitive Therapy and Research. 1986; 10(2):225–236.

Scherrer MC, Dobson KS. Mood-induced cognitive and emotional reactivity, life stress, and the prediction of depressive relapse. Journal of Clinical Psychology. 2009; 65(1):20–35. [PubMed: 19051242]

Segal ZV. Summary of relapse and recurrence from a cognitive perspective. Depressive Disorders: Index and Reviews. 1996; 1:3–17.

Segal ZV, Gemar Z, Williams S. Differential cognitive response to a mood challenge following successful cognitive therapy or pharmacotherapy for unipolar depression. Journal of Abnormal Psychology. 1999; 108(1):3–10. [PubMed: 10066988]

Segal ZV, Kennedy S, Gemar M, Hood K, Pedersen R, Buis T. Cognitive reactivity to sad mood provocation and the prediction of depressive relapse. Archives of General Psychiatry. 2006; 63(7): 749–755. [PubMed: 16818864]

Singer AR, Dobson KS. An experimental investigation of the cognitive vulnerability to depression. Behaviour Research and Therapy. 2007; 45(3):563–575. [PubMed: 16797484]

Solomon DA, Keller MB, Leon AC, Mueller TI, Lavori PW, Shea MT, et al. Multiple recurrences of major depressive disorder. American Journal of Psychiatry. 2000; 157(2):229–233. [PubMed: 10671391]

Stewart AL, Hays RD, Ware JE. The MOS short-term general health survey: Reliability and validity in patient populations. Medical Care. 1988; 26:724–735. [PubMed: 3393032]

Üstün TB, Ayuso-Mateos JL, Chatterji S, Mathers C, Murray CJL. Global burden of depressive disorders in the year 2000. The British Journal of Psychiatry. 2004; 184:386–392. [PubMed: 15123501]

Van der Does W. Cognitive Reactivity to Sad Mood: Structure and validity of a new measure. Behaviour Research and Therapy. 2002; 40:105–120. [PubMed: 11762423]

Vittengl JR, Clark LA, Dunn TW, Jarrett RB. Reducing relapse and recurrence in unipolar depression: A comparative meta-analysis of cognitive-behavioral therapy's effects. Journal of Consulting and Clinical Psychology. 2007; 75(3):475–488. [PubMed: 17563164]

Weissman AN. The Dysfunctional Attitudes Scale: A validation study (Doctoral dissertation, University of Pennsylvania, 1979). Dissertation Abstracts International. 1979; 40:1389B–1390B.

Wenze SJ, Gunthert KC, Forand NR. Influence of dysphoria on positive and negative cognitive reactivity to daily mood fluctuations. Behaviour Research and Therapy. 2007; 45:915–927. [PubMed: 17059811]

Westermann R, Spies K, Stahl G, Hesse FW. Relative effectiveness and validity of mood induction procedures: A meta-analysis. European Journal of Social Psychology. 1996; 26(4):557–580.

Williams JBW. A structured interview guide for the Hamilton Depression Rating Scale. Archives of General Psychiatry. 1988; 45(8):742–747. [PubMed: 3395203]

Zuckerman M, Lubin B. Normative data for the Multiple Affect Adjective Checklist. Psychological Reports. 1965; 16(2):438. [PubMed: 14285844]

Highlights

- We induced negative mood in patients treated for depression with cognitive therapy.
- We predicted that negative mood would result in cognitive reactivity.
- The mood induction did induce negative mood in 80% of patients.
- The hypothesized cognitive reactivity was not found.
- Patients with more unprimed dysfunctional attitudes were more likely to relapse/recur.

Table 1

Demographic and Clinical Characteristics of Sample at First Mood Induction Procedure (Blind Evaluation at End of Acute Phase Cognitive Therapy)

Characteristics	Total (*n*=207)	Mood Worsened (*n*=166)	Mood Improved (*n*=41)[a]
Demographic			
Sex No. (%) female	137(66.2)	115(69.3)	22(53.7)
Race No. (%) white	179 (86.5)	145(87.4)	34(82.9)
Age mean (SD)	42.9(11.9)	43.1(11.9)	42.1(12)
Marital Status No. (%)			
Single	119(57.5)	96(57.8)	23(56.1)
Partnered[b]	88(42.5)	70(42.2)	18(43.9)
Education mean (SD)	15.5(2.9)	15.5(2.8)	15.8(3.3)
Employment No. (%)			
Full-time	98(47.3)	78(47.0)	20(48.8)
Housework	16(7.7)	12(7.2)	4(9.8)
Other	11(5.3)	10(6.0)	1(2.4)
Part-time	26(12.6)	24(14.5)	2(4.9)
Retired	9(4.4)	7(4.2)	2(4.9)
Student	13(6.2)	11(6.6)	2(4.9)
Unemployed	34(16.4)	24(14.5)	10(24.4)
Clinical			
Age of onset mean (SD) in years	21.4(10.6)	21.4(10.5)	21(11.4)
Median	19	18.5	19
Length of current episode (SD) in months	21.6(33.1)	21.7(34.2)	21(28.6)
Median	8	8.5	6
Length of illness mean (SD) in years	21.1(11.5)	21.2(11.7)	20.5(10.8)
Median	20	21	18
Comorbidity of DSM-IV Diagnoses No. (%)			
Current	83(40.1)	66(39.8)	17(41.5)
Past	153(73.9)	122(73.5)	31(75.6)
Current Double Depression	10(4.8)	7(4.2)	3(7.3)
Depressive Subtype No. (%)			
DSM-IV Melancholia	75(36.2)	61(36.8)	14(34.1)
RDC endogenous, definite	76(36.7)	64(38.6)	12(29.3)

Note. *n* = Number; SD = Standard Deviation; $HRSD_{17}$ = Hamilton Rating Scale for Depression; DSM-IV = Diagnostic and Statistical Manual, 4th Edition; RDC = Research Diagnostic Criteria.

[a] N reduced to 39 for DSM-IV Melancholia, 40 for Endogenous Depression.

[b] Partnered refers to patients who are married or are living with a partner.

Table 2

Change in Mood at First Mood Induction Procedure (Blind Evaluation at End of Acute Phase Cognitive Therapy)

Mood Induction Sample	Mean (SD) VAS Score		F Statistic	*p*-value
	Pre MIP	Post MIP		
Full Sample (n = 207)	68.3 (16.9)	51.0 (20.2)	$F_{(1,206)} = 167.4$	<0.0001
Mood Worsened (n = 166)	70.0 (16.0)	47.6 (19.1)	$F_{(1,165)} = 250.5$	<0.0001
Mood Unchanged or Improved (n = 41)	61.6 (19.0)	64.7 (18.9)	$F_{(1,40)} = 38.7$	<0.0001

Note. n = Number; SD = Standard Deviation; MIP = Mood Induction Procedure; VAS = Visual Analogue Scale.

Table 3

Change in Dysfunctional Attitudes at First Mood Induction Procedure (Blind Evaluation at End of Acute Phase Cognitive Therapy)

Mood Induction Sample	Mean (SD) DAS Score		F Statistic	*p*-value
	Pre MIP	Post MIP		
Full Sample (n = 207)	113.2 (29.9)	113.6 (33.1)	$F_{(1,206)} = 0.1$	<0.760
Mood Worsened (n = 166)	112.7 (30.8)	115.0 (34.4)	$F_{(1,165)} = 2.3$	<0.134
Mood Unchanged or Improved (n = 41)	115.1 (26.8)	107.9 (26.8)	$F_{(1,40)} = 6.3$	<0.016

Note. n = Number; SD = Standard Deviation; MIP = Mood Induction Procedure; DAS = Dysfunctional Attitude Scale.

Table 4

Cox Proportional hazards regression model results for time to relapse/recurrence over 8, 20, and 32 Months.

Variable	Chi-square (1 df)	p-value	Hazard Ratio	95% Confidence Interval
8 Months				
$HRSD_{17}$ Score	0.31	.58	1.03	0.93, 1.13
Pre-MIP DAS Score	0.68	.41	1.01	0.99, 1.02
20 Months				
$HRSD_{17}$ Score	0.32	.57	1.02	0.95, 1.11
Pre-MIP DAS Score	3.93	.05	1.01	1.00, 1.02
32 Months				
$HRSD_{17}$ Score	2.89	0.09	1.07	0.99, 1.15
Pre-MIP DAS Score	4.01	0.05	1.01	1.00, 1.02

Table 5

Kaplan-Meier Estimates of Proportion Relapsed/Recurred over 8, 20, and 32 Months Post-randomization in Patients with Mood Unchanged/Improved and Mood Worsened after Mood Induction Procedure at the First Blind Evaluation.

Months	Mood Unchanged/Improved n = 41	Mood Worsened n = 166	Log-rank chi-square (p-value)
8 months	22.3 (7 of 41)	22.3 (30 of 166)	0.01 (0.906)
20 months	26.5 (8 of 41)	39.8 (49 of 166)	1.36 (0.244)
32 months	35.7 (10 of 41)	48.3 (57 of 166)	1.16 (0.281)